UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/523,682 | 02/01/2005 | Kirk Schnorr | 10292.204-US | 5935 |

25908 7590 07/17/2007
NOVOZYMES NORTH AMERICA, INC.
500 FIFTH AVENUE
SUITE 1600
NEW YORK, NY 10110

| EXAMINER | |
|---|---|
| STEELE, AMBER D | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1639 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 07/17/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/523,682 | SCHNORR, KIRK | |
| | Examiner | Art Unit | |
| | Amber D. Steele | 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *45-64* is/are pending in the application.

4a) Of the above claim(s) *48,50,51,55 and 61-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-47,49,52-54 and 56-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/1/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of the Claims*

1. The preliminary amendment received on February 1, 2005 canceled claims 1-44 and added new claims 45-64.

Claims 45-64 are currently pending.

Claims 45-47, 49, 52-54, and 56-60 are currently under consideration.

### *Election/Restrictions*

2. Applicant's election of Group I (claims 45-60) in the reply filed on April 30, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 61-64 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 30, 2007.

4. Applicant's election of bacterium as the species of microorganism and comprising a transposon as the species of DNA in the reply filed on April 30, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

5. Claims 48, 50-51, and 55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 30, 2007.

***Priority***

6. The present application claims status as a national stage (371) of PCT/DK03/00519 filed August 1, 2003 and claims foreign priority to Denmark PA 2002 01163 filed August 1, 2002.

7. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

***Information Disclosure Statement***

8. The information disclosure statement (IDS) submitted on February 1, 2005 is being considered by the examiner.

***Specification***

9. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

***Claim Objections***

10. Claim 57 is objected to because of the following informalities: the claim recites □-lactamase. β-lactamase is suggested. Appropriate correction is required.

***Invention as Claimed***

11. A method for isolating a polynucleotide that encodes a polypeptide of interest which comprises a signal sequence for secretion or partial secretion, the method comprising the

sequential steps of: (a) providing a DNA or cDNA library from an organism producing the polypeptide of interest, wherein the library is comprised in a circular vector and is produced in vitro without ultraviolet irradiation of the component polynucleotides; (b) amplifying the library by rolling circle amplification, thereby forming concatamers; (c) inserting into the library a DNA fragment comprising a promotorless and secretion signal-less polynucleotide encoding a secretion reporter; (d) introducing the amplified library comprising the inserted DNA fragment into a host cell, (e) screening for and selecting a host cell that secretes or partially secretes the active secretion reporter; and (f) identifying from the selected host cell the polynucleotide into which the secretion reporter was inserted, and isolating the polynucleotide' wherein steps (b) and (c) may be performed in any order and variations thereof.

***Claim Rejections - 35 USC § 112***

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 45-47, 49, 52-54, and 56-60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 USC 112, first paragraph "Written Description" requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a **written description** rejection.

Claim 45 is drawn to a method for isolating a polynucleotide that encodes a polypeptide of interest which comprises a signal sequence for secretion or partial secretion, the method comprising the sequential steps of: (a) providing a DNA or cDNA library from an organism producing the polypeptide of interest, wherein the library is comprised in a circular vector and is produced in vitro without ultraviolet irradiation of the component polynucleotides; (b) amplifying the library by rolling circle amplification, thereby forming concatamers; (c) inserting into the library a DNA fragment comprising a promotorless and secretion signal-less polynucleotide encoding a secretion reporter; (d) introducing the amplified library comprising the inserted DNA fragment into a host cell, (e) screening for and selecting a host cell that secretes or partially secretes the active secretion reporter; and (f) identifying from the selected host cell the polynucleotide into which the secretion reporter was inserted, and isolating the polynucleotide' wherein steps (b) and (c) may be performed in any order. The invention as claimed encompasses all known cDNA, vectors, reporters, polypeptides, host cells, etc. and all potential cDNA, vectors, reporters, polypeptides, host cells, etc. since all cDNA encodes polypeptides (i.e. exon segments), any reporter/polypeptide can be a reporter (i.e. dependent on reagents available to detect), any vector can be circularized and amplified, virtually any host cell can be transfected, etc. The claimed invention states that the circular vector must be produced in vitro without ultraviolet irradiation and the secretion reporter must be "active" for screening (i.e. functional limitations). The claimed invention does not include any structural information regarding the DNA, cDNA, or polypeptide of interest except that the DNA or cDNA encodes the polypeptide of interest. In addition, the claimed invention does not include any structural information regarding how a secretion reporter without a promoter or a secretion signal would be

expressed and secreted. Thus, various functional limitations are utilized to define the reagents necessary to perform the method as claimed without providing structural information.

The specification teaches "laundry lists" of potential host cells (please refer to pages 10-13), potential promoters, and potential elements of the vector (please refer to pages 16-19). In addition, the specification teaches that the DNA or cDNA library may be from an environmental sample or microorganism and the vector may be any vector with various generic components (please refer to pages 6-8). Furthermore, the specification teaches the pMhas5 vector with kanamycin resistance, β-gal, shine dalgarno sequence, lac promoter, KanP1 primer; E. coli as the host cell; SEQ ID NO: 1 as the DNA; cDNA library from *R. pusillus*; and SigA2 transposon (please refer to pages 21-25). Therefore, one skilled in the relevant art would not reasonably conclude that the Applicants had possession of the scope of the invention as claimed because the specification does not teach a representative number of species of the various claimed genuses utilized in the method. A lack of adequate written description issue arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species; see MPEP §2163).

See Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was *in possession of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow

persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See page 1116.).

With the exception of pMhas5 vector with kanamycin resistance, β-gal, shine dalgarno sequence, lac promoter, KanP1 primer; E. coli as the host cell; SEQ ID NO: 1 as the DNA; cDNA library from *R. pusillus*; and SigA2 transposon as disclosed by the specification at pages 21-25, the skilled artisan cannot envision the method of claim 45. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class wherein the specification provided only the bovine sequence.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 45-47, 49, 52-54, and 56-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The limitations that the inserted polynucleotide (encoding secretion reporter) of method step (c) must be promoterless and secretion signal-less are indefinite. One of ordinary skill in the art would not be able to determine the scope of the presently claimed invention. For example, is the new polynucleotide insert (encoding secretion reporter) only promoterless and secretion signal-less, is the new polynucleotide insert (encoding secretion reporter) operably linked to a promoter and secretion signal within the vector (if not,

how is the secretion reporter polypeptide produced and secreted), does recombination have to occur in order for the new polynucleotide insert (encoding secretion reporter) to be expressed and secreted, etc.?

16. Claim 46 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "normalized" is indefinite. One of ordinary skill in the art would not be able to determine the scope of the presently claimed invention. For example, what is the DNA or cDNA library normalized to, is a housekeeping gene or housekeeping library necessary, does normalized relate to the amount of DNA or cDNA in the library or the number of constructs, does normalized relate to the transfection efficiency, does normalized relate to the amount of polypeptide produced, etc.?

***Claim Rejections - 35 USC § 103***

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 45-47, 49, 52-54, and 56-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duffner et al. U.S. Patent 7,029,842 published June 20, 2002 and Fire et al. U.S. Patent 5,648,245 issued July 15, 1997. Please note: the Fire et al. reference was provided by applicant in the IDS.

For present claim 45, Duffner et al. teach methods for isolating and identifying a polynucleotide comprising (a) providing a DNA or cDNA library from an organism within a circular vector produced in vitro (i.e. without ultraviolet irradiation due to silence of the reference with regard to UV irradiation), (b) gene amplification and PCR, (c) inserting a DNA fragment comprising a promoterless and secretion signal-less polynucleotide encoding a secretion reporter, (d) transfection of host cells with the vector, (e) screening for the secretion reporter, and (f) identifying and isolating the polynucleotide (please refer to entire specification particularly the abstract; columns 1-4, 6, 9-11, 13-15, 18-20; Examples 1-9; claims).

For present claim 46, Duffner et al. teach normalizing the DNA or cDNA library (please refer to entire specification particularly column 14).

For present claim 47, Duffner et al. teach deriving the DNA or cDNA library from a microorganism (please refer to entire specification particularly column 14).

For present claim 49, Duffner et al. teach bacterium as the microorganism (please refer to entire specification particularly column 14).

For present claim 52, Duffner et al. teach restriction enzyme cleavage sites and recombination recognition sites (please refer to entire specification particularly columns 6, 9-10).

For present claim 53, Duffner et al. teach in vitro (please refer to entire specification particularly the abstract; columns 1-2; Examples 1-9).

For present claim 54, Duffner et al. teach transposons (please refer to entire specification particularly columns 1-4, 9, 14, 19; Examples 1-9).

For present claim 56, Duffner et al. teach secretion reporters which allow the cell to grow in the presence of a substance which otherwise inhibits cell growth (please refer to entire specification particularly paragraph spanning columns 14 and 15).

For present claim 57, Duffner et al. teach β-lactamase and invertase (please refer to entire specification particularly columns 1-2, 4, 15, 20; Examples 1-9).

For present claim 58, Duffner et al. teach N-terminal peptide linker comprising a specific target site for proteolytic cleavage (please refer to entire specification particularly column 15).

For present claim 59, Duffner et al. teach linear vectors and circularized vectors (i.e. monomers, not concatamers; please refer to entire specification particularly columns 9-10).

For present claim 60, Duffner et al. teach restriction enzyme recognition sites, restriction enzyme digestion, and circularized vectors wherein ligation is utilized after restriction enzyme digestion (please refer to entire specification particularly columns 6, 9-10; Examples 1-9).

However, Duffner et al. does not specifically teach RCA or rolling circle amplification.

For present claims 45, 59, and 60, Fire et al. teach in vitro methods for constructing, screening, and identifying oligonucleotides comprising (a) providing an oligonucleotide library, (b) rolling circle amplification to form concatamers, (c) utilizing a reporter gene, (d) utilizing expression vectors and host cells, (e) screening, and (f) identifying the oligopnucleotides and teach utilizing restriction enzyme cleavage to produce monomers from the concatamers (please refer to entire specification particularly the abstract; columns 1-5; Examples 3-5 and 7-9).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the signal sequence trapping methods taught by Duffner et al. with the rolling circle replication methods taught by Fire et al.

One having ordinary skill in the art would have been motivated to do this because Fire et al. teach that many plasmids and viruses utilize rolling circle amplification to replicate (please refer to column 2). In addition, Fire et al. teach that the rolling circle amplification can be utilized in in vitro evolution methods to screen for select molecules with defined biological or chemical properties (please refer to column 1). Furthermore, the method of amplification would be an experimental design choice.

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the signal sequence trapping methods taught by Duffner et al. with the rolling circle replication methods taught by Fire et al. because of the various examples taught by Duffner et al. (Examples 1-9) and Fire et al. (Examples 1-9).

Therefore, the modification of the signal sequence trapping methods taught by Duffner et al. with the rolling circle replication methods taught by Fire et al. render the instant claims *prima facie* obvious.

19. Claims 45-47, 49, 52-54, and 56-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duffner et al. WO 01/77315 published October 18, 2001 and Fire et al. U.S. Patent 5,648,245 issued July 15, 1997. Please note: both references were provided by applicant in the IDS.

For present claim 45, Duffner et al. teach methods for isolating and identifying a polynucleotide comprising (a) providing a DNA or cDNA library from an organism within a circular vector produced in vitro (i.e. without ultraviolet irradiation due to silence of the reference with regard to UV irradiation), (b) gene amplification and PCR, (c) inserting a DNA

fragment comprising a promoterless and secretion signal-less polynucleotide encoding a secretion reporter, (d) transfection of host cells with the vector, (e) screening for the secretion reporter, and (f) identifying and isolating the polynucleotide (please refer to entire specification particularly the abstract; pages 1-4, 10-19, 23-24; Examples 1-9).

For present claim 46, Duffner et al. teach normalizing the DNA or cDNA library (please refer to entire specification particularly page 16).

For present claim 47, Duffner et al. teach deriving the DNA or cDNA library from a microorganism (please refer to entire specification particularly page 16).

For present claim 49, Duffner et al. teach bacterium as the microorganism (please refer to entire specification particularly page 16).

For present claim 52, Duffner et al. teach restriction enzyme cleavage sites and recombination recognition sites (please refer to entire specification particularly pages 11, 17-18).

For present claim 53, Duffner et al. teach in vitro (please refer to entire specification particularly the abstract; page 16; Examples 1-9).

For present claim 54, Duffner et al. teach transposons (please refer to entire specification particularly pages 1-4, 16, 23; Examples 1-9).

For present claim 56, Duffner et al. teach secretion reporters which allow the cell to grow in the presence of a substance which otherwise inhibits cell growth (please refer to entire specification particularly page 17).

For present claim 57, Duffner et al. teach β-lactamase and invertase (please refer to entire specification particularly pages 2, 4, 17, 24; Examples 1-9).

For present claim 58, Duffner et al. teach N-terminal peptide linker comprising a specific target site for proteolytic cleavage (please refer to entire specification particularly pages 17-19).

For present claim 59, Duffner et al. teach linear vectors and circularized vectors (i.e. monomers, not concatamers; please refer to entire specification particularly pages 10-12).

For present claim 60, Duffner et al. teach restriction enzyme recognition sites, restriction enzyme digestion, and circularized vectors wherein ligation is utilized after restriction enzyme digestion (please refer to entire specification particularly page 11, 17-18; Examples 1-9).

However, Duffner et al. does not specifically teach RCA or rolling circle amplification.

For present claims 45, 59, and 60, Fire et al. teach in vitro methods for constructing, screening, and identifying oligonucleotides comprising (a) providing an oligonucleotide library, (b) rolling circle amplification to form concatamers, (c) utilizing a reporter gene, (d) utilizing expression vectors and host cells, (e) screening, and (f) identifying the oligopnucleotides and teach utilizing restriction enzyme cleavage to produce monomers from the concatamers (please refer to entire specification particularly the abstract; columns 1-5; Examples 3-5 and 7-9).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the signal sequence trapping methods taught by Duffner et al. with the rolling circle replication methods taught by Fire et al.

One having ordinary skill in the art would have been motivated to do this because Fire et al. teach that many plasmids and viruses utilize rolling circle amplification to replicate (please refer to column 2). In addition, Fire et al. teach that the rolling circle amplification can be utilized in in vitro evolution methods to screen for select molecules with defined biological or

chemical properties (please refer to column 1). Furthermore, the method of amplification would be an experimental design choice.

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the signal sequence trapping methods taught by Duffner et al. with the rolling circle replication methods taught by Fire et al. because of the various examples taught by Duffner et al. (Examples 1-9) and Fire et al. (Examples 1-9).

Therefore, the modification of the signal sequence trapping methods taught by Duffner et al. with the rolling circle replication methods taught by Fire et al. render the instant claims *prima facie* obvious.

***Future Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ADS
June 26, 2007

MARK L. SHIBUYA
PRIMARY EXAMINER